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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,318	COSGROVE, DOMINIC E.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claims 1, 8, 15 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In claims 1, 8, and 15, applicant recites antibodies immunoreactive with at least a portion of a human usherin protein having SEQ ID NO: 4 wherein the antibody does not cross react with other non-usherin proteins within the biological sample. In the specification, however, applicant has only disclosed antibodies immunoreactive with SEQ ID NOs: 1, 2, and 4, and has only provided working examples of antibodies immunoreactive with SEQ ID NOs: 1 and 2. In the case of SEQ ID NO: 2, the antibody is disclosed as preferably immunoreacting with the LN domain of the usherin protein (p.17, lines 10-11). However, applicant also discloses that the LN

module is a common feature of laminins, found in six of the known chains (p.12, lines 20-25). Laminins are further disclosed as being one of the major components forming the extracellular matrix of basement membranes in all tissues (p.12, lines 5-9). Therefore, antibodies disclosed by applicant that immunoreact with SEQ ID NO: 2 would also immunoreact with laminins. In addition, there is no evidence provided by applicant that would suggest that the antibodies that immunoreact with SEQ ID NOs: 1 and 2 would not cross-react with non-usherin proteins within the biological sample. Neither has applicant provided epitopes of SEQ ID NOs: 1, 2, 4 that are specific only to the usherin protein, rendering it unclear how antibodies that are immunoreactive to the usherin protein and not cross-reactive with non-usherin proteins would be obtained.

4. Claims 1, 8, 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not reasonably provide enablement for a method of determining whether an individual is at risk for developing Usher syndrome Type IIa.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 1, 8, and 15 are broadly drawn to a method comprising the step of incubating a biological sample with any antibody immunoreactive with a portion of a protein having SEQ ID NO: 4 and that does not cross-react with non-usherin proteins within the biological sample. However, applicant fails to teach how such antibodies would be obtained. Neither does applicant specify which epitopes of SEQ ID NO: 4 are unique to the usherin protein so that antibodies specific only to usherin protein can be made.

While applicant does provide working examples of antibodies immunoreactive with SEQ ID NOs: 1 and 2 (p. 22, example 1), it is unclear the specificity of the antibodies toward the sequences, and if the antibodies selectively recognize the usherin protein epitopes, and where the epitopes are located. In addition, applicant does not provide any data involving the use of the antibodies in tissue samples from individuals with Usher syndrome Type IIa, rendering it unclear how well the antibodies would perform in determining individuals having or being at risk for Usher syndrome Type IIa.

There is also no evidence provided by applicant that would suggest that the antibodies that immunoreact with SEQ ID NOs: 1 and 2 would not cross-react with non-usherin proteins within the biological sample. Neither has applicant provided epitopes of SEQ ID NOs: 1, 2, 4 that are specific only to the usherin protein, rendering it unclear how antibodies that are immunoreactive to the usherin protein and not cross-reactive with non-usherin proteins would be obtained. In fact, in the case of SEQ ID NO: 2, the antibody is disclosed as preferably immunoreacting with the LN domain of the usherin protein (p.17, lines 10-11). However, applicant also discloses that the LN module is a common feature of laminins, found in six of the known chains (p.12, lines 20-25). Laminins are further disclosed as being one of the major

components forming the extracellular matrix of basement membranes in all tissues (p.12, lines 5-9). Therefore, antibodies disclosed by applicant that immunoreact with SEQ ID NO: 2 would also immunoreact with laminins, which are present in all tissues.

In the specification, applicant further states that the methods of the present invention also provide for the use of antibodies that are immunoreactive with an usherin protein encoded by the USH2A gene, as well as other polypeptides (16, lines 22-25). If the antibody forms an immunoconjugate with other polypeptides, false negatives would potentially be generated, as immunoconjugates would be present even though the usherin protein is not.

Although applicant states that the antibodies preferably selectively recognize the usherin protein epitopes and bind to these epitopes with high affinity (p. 16, lines 25-30), applicant fails to specify any epitopes, nor does the applicant teach how to create antibodies that would be capable of binding to the epitopes in the protein with high affinity, rendering it unclear how a person of ordinary skill in the art would be able to do so. Furthermore, in the claims, applicant merely requires that an antibody that is immunoreactive with a portion of a human usherin protein, and does not limit the antibodies to specific epitopes or regions of the protein.

Furthermore in regard to claim 1 and 15, applicant teaches that there is likely some percentage of individuals with Usher syndrome Type IIa that continue to express immunoreactive usherin in their tissues (p.15, lines 9-16). Applicant, however, has not specified what percentage of individuals would continue to do so, rendering it unclear what the accuracy of the method and level of predictability would be in determining whether an individual would have or be at risk for developing Usher syndrome Type IIa.

As applicant has pointed out, previous results have also suggested that usherin might have very restricted tissue distribution (p.37, lines 25-30) (p.1755, cols. 1-3, [Eudy et al, Mutation of a gene encoding a protein with extracellular matrix motifs in usher syndrome type IIa, 1998, Science, 280, 1753-1757]). While applicant teaches that usherin is expressed in the basement membranes of a large number of tissues in mice (p. 38, lines 3-10), applicant has only established that usherin is associated with the basement membranes of the retina in humans (p. 38, lines 28-30). Furthermore, applicant does not show the distribution or detection of usherin, in samples in the diseased state, from individuals having Usher syndrome Type IIa. Although applicant has amended the claims to samples from tissues that normally include the usherin protein in an individual not having Usher syndrome Type IIa, applicant has not disclosed how prevalent the usherin protein is in the tissue, or the use of controls to ensure that any usherin protein present in the tissue will immunoreact with the antibodies.

Neither has applicant provided any studies testing the effectiveness of the method in determining the presence nor the risk of developing Usher syndrome Type IIa, rendering it unclear how successful the method is in determining the presence of Usher syndrome Type IIa.

The specification does not teach a method of determining whether an individual has or is at risk for developing Usher syndrome type IIa using antibodies that bind only a portion of a human usherin protein having SEQ ID NO:4. Insufficient direction or guidance and no working examples are provided to assist one skilled in the art to make and use antibodies to perform a method of determining whether an individual is at risk for developing Usher syndrome Type IIa as recited in claims 1-23.

Response to Arguments

5. Applicant's arguments on pgs 9-11 with respect to the rejection of claims 1-23 under the 35U.S.C. 112, first paragraph in regard to the written description requirement have been considered but are moot in view of the new ground(s) of rejection.

6. Applicant's arguments filed on pgs 12-14 with respect to the rejection of claims 1-23 under the 35U.S.C. 112, first paragraph, in regard to the enablement requirement have been fully considered but they are not persuasive. While applicant requires that the antibodies be immunoreactive with usherin protein and not cross react with non-usherin proteins, applicant fail to provide guidance for producing such antibodies. In fact, in the case of antibodies disclosed by applicant for immunoreacting with SEQ ID NO: 2, the antibody is disclosed as preferably immunoreacting with the LN domain of the usherin protein (p.17, lines 10-11). However, applicant also discloses that the LN module is a common feature of laminins, found in six of the known chains (p.12, lines 20-25). Laminins are further disclosed as being one of the major components forming the extracellular matrix of basement membranes in all tissues (p.12, lines 5-9). Therefore, antibodies disclosed by applicant that immunoreact with SEQ ID NO: 2 would also immunoreact with laminins. Applicant also fails to show how the antibodies used would be established as not being cross-reactive with non-usherin proteins, or specify epitopes unique to the usherin protein that would allow antibodies specific only to the usherin protein to be produced.

With respect to applicant's arguments on page 13 that the examiner appears to be inappropriately reading the specification into the claims, it should be noted that the claims must be read in light of the specification. As applicant has pointed out the antibodies would be immunoreactive with the usherin protein... as well as other polypeptides, which would

potentially generate false negatives. Applicant also argues that that the method evaluate for the absence of an antibody-usherin protein immunoconjugate and correlate such an absence with the individual having or being at risk for developing Usher syndrome IIa. However, as applicant has pointed out, usherin distribution in some tissues is very restricted, which could potentially generate false positives. This raises the question whether the method would actually be useful in determining whether an individual has or is at risk for developing Usher syndrome Type IIa, particularly since applicant has not provided any studies showing how effective the method is.

Applicant's arguments on page 14 with respect to claims 8-14 that the claims are drawn to a method of detecting the presence or absence of an usherin protein are correct, and that portion of the rejection has been withdrawn with respect to claims 8-14.

With respect to applicant's argument that applicant's amendment of "wherin the biological sample is from a tissue that normally includes the usherin protein in an individual not having Usher syndrome Type IIa" would render the limited tissue distribution concern moot is not found entirely persuasive. In particular, applicant has not disclosed how prevalent the usherin protein is in the tissue, or the use of controls to ensure that any usherin protein present in the tissue will immunoreact with the antibodies.

It should be noted that while this method may very well be effective in determining whether an individual has or is at risk for developing Usher syndrome Type IIa, applicant has not provided any studies or experimental data that would support this assertion, or provided sufficient guidance such that studies on the effectiveness of the method could be performed without undue experimentation.

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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1/20/05